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(21) International Application Number: PCT/US98/17922 (22) International Filing Date: 28 August 1998 (28.08.98) (30) Priority Data: 60/057,394 29 August 1997 (29.08.97) US		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(71) Applicant: ONTOGENY, INC. [US/US]; 45 Moulton Street, Cambridge, MA 02138 (US). (72) Inventors: BLADGEN, Chris, S.; 26-29 Drury Lane, London WC2B 5RL (GB). CURRIE, Peter, D.; 26-29 Drury Lane, London WC2B 5RL (GB). INGHAM, Philip, W.; Firth Court, Western Bank, Sheffield S10 2TN (GB). HUGHES, Simon, M.; 26-29 Drury Lane, London WC2B 5RL (GB). (74) Agents: VINCENT, Matthew, P. et al.; Foley, Hoag & Eliot LLP, One Post Office Square, Boston, MA 02109 (US).		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
		(88) Date of publication of the international search report: 27 May 1999 (27.05.99)	
(54) Title: REGULATION OF MUSCLE TISSUES BY HEDGEHOG-LIKE POLYPEPTIDES, AND FORMULATIONS AND USES RELATED THERETO			
(57) Abstract			
<p>The present application relates to a method for modulating the formation and/or maintenance of muscle tissue by ectopically contacting muscle cells, especially muscle stem/progenitor cells, <i>in vitro</i> or <i>in vivo</i>, with a hedgehog therapeutic or ptc therapeutic in an amount effective to alter the growth state of the treated cells, e.g., relative to the absence of administration of the hedgehog therapeutic or ptc therapeutic.</p>			

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INTERNATIONAL SEARCH REPORT

Internati. Application No
PCT/US 98/17922

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 6	A61K38/17	A61K31/00	A61K31/47	A61K31/495	A61K31/55
	A61K31/70	C12N5/00		//A61K48/00, C07K14/46, C12N15/11,	
			C12N15/12, C07H21/04		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	<p>WO 98 48830 A (BORYCKI ANNE GAELLE ;EMERSON CHARLES P (US); UNIV PENNSYLVANIA (US) 5 November 1998</p> <p>see abstract</p> <p>see page 3, line 4 – line 15</p> <p>see page 9, line 19 – line 31; claims;</p> <p>figures IA,2,4; examples</p> <p>---</p>	1-7, 25-32
P,X	<p>C.S. BLAGDEN ET AL.: "NOTOCHORD INDUCTION OF ZEBRAFISH SLOW MUSCLE MEDIATED BY SONIC HEDGEHOG"</p> <p>GENES AND DEVELOPMENT,</p> <p>vol. 11, no. 17, 1 September 1997, pages 2163-2175, XP002098537</p> <p>see the whole document</p> <p>---</p> <p>---</p>	1-7, 25

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

31 March 1999

Date of mailing of the international search report

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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Internati- Application No
PCT/US 98/17922

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	D. DUPREZ ET AL.: "SONIC HEDGEHOG INDUCES PROLIFERATION OF COMMITTED SKELETAL MUSCLE CELLS IN THE CHICK LIMB" DEVELOPMENT, vol. 125, no. 3, February 1998, pages 495-505, XP002098538 see the whole document ---	1-7,25
X	WO 97 04761 A (UNIV BOSTON) 13 February 1997 see abstract see page 6, line 4 - line 12 see page 17, line 4 - line 10; claims ---	1,8-12, 18-20, 23,25, 26,31,32
X	L.M. WASSERMAN ET AL.: "cAMP EFFECTS ON MYOGENIC GENE EXPRESSION IN RHYABDOMYOSARCOMA CELLS" EXPERIMENTAL CELL RESEARCH, vol. 227, no. 1, 1996, pages 55-62, XP002098539 see the whole document ---	1,8-12, 18, 21-26, 31,32
X	A.E. MÜNSTERBERG ET AL.: "COMBINATORIAL SIGNALING BY SONIC HEDGEHOG AND Wnt FAMILY MEMBERS INDUCES MYOGENIC bHLH GENE EXPRESSION IN THE SOMITE" GENES AND DEVELOPMENT, vol. 9, no. 23, 1995, pages 2911-2922, XP002098540 see the whole document ---	1-7,25
X	S.H. DEVOTO ET AL.: "ZEBRAFISH MUSCLE FIBER TYPE DEVELOPMENT IS REGULATED BY COMPETING INFLUENCES OF HEDGEHOG AND TGF-beta GENE FAMILY MEMBERS" DEVELOPEMNT BIOLOGY, vol. 186, no. 2, June 1997, page 321 XP002098541 see abstract no. B63 ---	1-7,25
X	P.D. CURRIE ET AL.: "INDUCTION OF A SPECIFIC MUSCLE CELL TYPE BY A HEDGEHOG-LIKE PROTEIN IN ZEBRAFISH" NATURE, vol. 382, no. 6590, 1996, pages 452-455, XP002098542 cited in the application see the whole document ---	1-7,25
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INTERNATIONAL SEARCH REPORT

Internati- Application No
PCT/US 98/17922

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAMMERSCHMIDT M ET AL: "Protein kinase A is a common negative regulator of Hedgehog signaling in the vertebrate embryo" GENES AND DEVELOPMENT, vol. 10, no. 6, 15 March 1996, pages 647-658, XP002092607 see abstract see page 655 - page 656 ---	1-7,25
A	E.J. AW ET AL.: "MYOGENESIS IN VITRO. ENHANCEMENT BY DIBUTYRYL cAMP" EXPERIMENTAL CELL RESEARCH, vol. 83, no. 2, 1974, pages 436-438, XP002098543 see the whole document ---	19-22
X	K. STYGALL ET AL.: "THE EFFECT OF CHOLERA TOXIN ON MYOGENESIS IN RAT SKELETAL MUSCLE CULTURES" DEVELOPMENTAL BIOLOGY, vol. 78, no. 1, 1980, pages 14-24, XP002098544 see the whole document ---	1,8-12, 21,22,25
X	WO 95 18856 A (HARVARD COLLEGE ;IMP CANCER RES TECH (GB)) 13 July 1995 cited in the application see abstract see page 3, line 18 - page 7, line 24 see page 55, line 15 - page 64, line 19; claims ---	24
A	WO 96 17924 A (UNIV JOHNS HOPKINS MED ;UNIV WASHINGTON (US)) 13 June 1996 cited in the application see the whole document ---	1-7, 25-32
A	DE 39 42 114 A (HIDAKA HIROYOSHI ;TOBISHI PHARMACEUTICAL CO (JP)) 28 June 1990 see abstract see page 83, line 39 - line 40; claims; example 200 -----	19,20

International application No.

PCT/US 98/17922

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim(s) 1-23, 52-32 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
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Remark on Protest

- The additional search fees were accompanied by the application.
 No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the large number of compounds which are theoretically contained within the definitions "ptc therapeutic", "small organic molecule", "protein kinase A inhibitor" and "antagonist of patched" of claims 1-13,17,18 and 24, the search had to be restricted on economic ground to the general idea of the invention and to the compounds mentioned in claims 20 and 22 (Art.6 PCT; Guidelines Chapt.II.7 last sentence and Chapt.III,3.7).

Claims searched completely: 16,20,22

Claims searched incompletely: 1-15,17-19,21,23-32

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat:	Application No
PCT/US 98/17922	

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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